

AMENDMENTS TO THE CLAIMS

1-34 (canceled).

35. (currently amended) A once a day oral pharmaceutical tablet ~~dosage form~~ consisting essentially of:

(a) a controlled release metformin core consisting essentially of:

(i) a compressed mixture of:

(A) 50-98% of metformin hydrochloride;

(B) 0.1-40% of a binding agent;

(C) 0-20% of an absorption enhancer; and

(D) 0-5% of a lubricant;

~~a mixture of metformin or a pharmaceutically acceptable salt thereof and at least one pharmaceutically acceptable excipient;~~

(ii) optionally a secondary seal coat surrounding the metformin mixture and

(iii) a semipermeable membrane surrounding the metformin mixture or the secondary seal coat if present consisting essentially of:

(A) 50-99% of a polymer that is permeable to the passage of water and aqueous biological fluids and is impermeable to the passage of metformin;

(B) 0-40% of a flux enhancer and

(C) 0-25% of a plasticizer, said membrane having at least one passageway formed therein for release of the metformin;

(b) a primary seal coat that does not contain an active pharmaceutical ingredient, that rapidly disperses or dissolves in water and that is applied to the semipermeable membrane of the controlled release metformin core; and

(c) an immediate release pioglitazone coating applied to the primary seal coat consisting essentially of comprising:

(i) pioglitazone hydrochloride; ~~or a pharmaceutically acceptable salt thereof;~~
and

(ii) a binder; and

(iii) a pore former

wherein the ~~tablet dosage form~~ exhibits the following metformin dissolution profile when tested in a USP Type 2 apparatus at 75 rpms in 900 ml of simulated intestinal fluid and 37°C: 20-40 ~~10-45~~% of the metformin is released after four hours; 45-90 ~~30-90~~% of metformin is released after eight hours and the following pioglitazone dissolution profile when tested in a USP apparatus Type 1 apparatus at 100 rpm in a pH 2.0 HCl-0.3M KCl buffer solution: at least 79% of the pioglitazone is released ~~release~~ after 20 minutes and at least 95% of the pioglitazone is release from the ~~tablet dosage form~~ after 30 minutes.

36. (canceled)

37. (currently amended) The ~~tablet dosage form~~ of claim ~~36~~ 35 wherein the ~~osmotic~~ tablet consists essentially of:

(i) a mixture of:

(A) 75-95 ~~50-98~~% of said metformin hydrochloride ~~or a pharmaceutically acceptable salt thereof~~;

(B) 3-15 ~~0.1-40~~% of a binding agent;

(C) 2-10 ~~0-20~~% of an absorption enhancer; and

(D) 0.5-1 ~~0-5~~% of a lubricant;

(ii) optionally a secondary seal coat surrounding the mixture; and

(iii) a semipermeable membrane consisting essentially of:

(A) 75-95 ~~50-99~~% of a polymer selected from the group consisting of ethylcellulose, cellulose esters, cellulose diesters, cellulose triesters, cellulose ethers, cellulose ester-ether, cellulose acylate, cellulose diacylate, cellulose triacylate, cellulose acetate, cellulose diacetate, cellulose triacetate, cellulose acetate propionate and cellulose acetate butyrate;

(B) 2-20 ~~0-40~~% of a flux enhancer and

(C) ~~2-15~~ 0-25% of a plasticizer, said membrane having at least one passageway formed therein for release of the metformin or a pharmaceutically acceptable salt thereof.

38. (canceled)

39. (currently amended). The tablet ~~dosage form~~ of claim 35 wherein the release of the metformin ~~or a pharmaceutically acceptable salt thereof~~ is not regulated by an expanding polymer.

40. (currently amended) The tablet ~~dosage form~~ of claim 35 wherein said controlled release of said metformin ~~or a pharmaceutically acceptable salt thereof~~ provides a Tmax of 8-12 hours.

41. (canceled).

42. (currently amended) The tablet ~~dosage form~~ of claim 41 wherein said release of the pioglitazone provides a Tmax of 1-4 hours.

43. (canceled).

44. (currently amended) The tablet ~~dosage form~~ of claim 35 wherein the pioglitazone coating is applied to the primary seal coating using a solvent mixture of water and an organic solvent.

45-46 (canceled).

47. (new) A once a day oral pharmaceutical tablet consisting of (a) a core; (b) a primary seal coat; (c) an immediate release pioglitazone coating; and (d) optionally an aesthetic coating wherein:

the core (a) consists of:

- (i) a compressed mixture of:
 - (I) 50-98% of metformin hydrochloride;
 - (II) 0.1-40% of a binding agent;
 - (III) 0-20% of an absorption enhancer; and
 - (IV) 0-5% of a lubricant;
- (ii) optionally a secondary seal coat surrounding the compressed mixture; and
- (iii) a semipermeable membrane consisting essentially of:
 - (I) 50-99% of a polymer selected from the group consisting of ethylcellulose, cellulose esters, cellulose diesters, cellulose triesters, cellulose ethers, cellulose ester-ether, cellulose acylate, cellulose diacylate, cellulose triacylate, cellulose acetate, cellulose diacetate, cellulose triacetate, cellulose acetate propionate and cellulose acetate butyrate;
 - (II) 0-40% of a flux enhancer; and
 - (III) 0-25% of a plasticizer, said membrane having at least one passageway formed therein for release of the metformin;

the primary seal coat (b) is applied to the semipermeable membrane (iii), does not contain an active pharmaceutical ingredient and rapidly disperses or dissolves in water;

the immediate release pioglitazone coating (c) consists of:

- (i) 0.1-20% based upon the total weight of the tablet of pioglitazone hydrochloride;
- (ii) 0.1-30% based upon the total weight of the tablet of a binder;
- (iii) 0-25% based upon the total weight of the tablet of a pore former; and
- (iv) 0-20% based upon the total weight of the tablet of a surfactant;

wherein the immediate release pioglitazone coating (c) is applied to the primary seal coat (b) that is applied to the semipermeable membrane (a)(iii) of the core (a);

the tablet provides a Tmax of 8-12 hours for the metformin and a Tmax of 1-4 hours for the pioglitazone:

the tablet exhibits the following metformin dissolution profile when tested in a USP Type 2 apparatus at 75 rpms in 900 ml of simulated intestinal fluid and 37°C:

0-15% of the metformin is released after two hours;

20-40% of the metformin is released after four hours;

45-90% of metformin is released after eight hours; and

not less than 60% of the metformin is released after twelve hours;

and the tablet exhibits the following pioglitazone dissolution profile when tested in a USP apparatus Type 1 apparatus at 100 rpm in a pH 2.0 HCl-0.3M KCl buffer solution:

at least 79% of the pioglitazone is released after 20 minutes and

at least 95% of the pioglitazone is release after 30 minutes.

48. (new) The tablet of claim 47 wherein the immediate release pioglitazone coating is applied to the primary seal coating using a solvent mixture of water and an organic solvent.

49. (new) The tablet of claim 47 wherein the compressed mixture of the core consists of::

(I) 75-95% of metformin hydrochloride;

(II) 3-15% of a binding agent;

(III) 2-10% of an absorption enhancer; and

(IV) 0.5-1% of a lubricant.

50. (new) The tablet of claim 35 wherein the polymer of the semipermeable membrane is cellulose acetate.

51. (new) The tablet of claim 47 wherein the polymer of the semipermeable membrane is cellulose acetate.